

## **REMARKS**

Reconsideration of the present application is requested in view of the foregoing amendments and following remarks.

### **I. Claim Numbering**

As noted in the previous Response, dated September 19, 2008, Applicants had inadvertently renumbered the claims in the Response to the Second Restriction Requirement filed on December, 21 2007. Applicants have since corrected the error and have numbered the claims to reflect the claim numbers provided in the application as filed; however, it appears that that the Examiner has referred to the incorrect number in the most recent Office Action, dated January 27, 2009.

Applicants refer to the correct claim numbers when addressing the rejections.

### **II. Claim Amendments**

Claims 4 and 8 are amended to delete the language "near a subsite." Support for the amendments can be found, e.g., at page 16, line 32 – page 17, line 2, of the original specification.

Claims 9 and 10 are amended to delete the recitation of GenBank Accession Nos.

Claim 33 is amended to change its dependency to provide antecedent basis for the term "lectin."

No new matter is added by these amendments.

Following entry of the amendments, Claims 1-5, 8-10, 19-23, 25-26, 32-40, 44-47, 56-60, 62-63, and 69-73 will be pending in the application with Claims 37-40, 44-47, 56-60, 62-63, and 69-73 withdrawn and Claims 6, 7, 11-18, 24, 27-31, 41-43, 48-55, 61, 64-68 and 74-145 cancelled without prejudice.

### **III. Rejections under 35 U.S.C. §112, second paragraph**

Claims 4<sup>1</sup> and 8<sup>2</sup> were rejected under 35 U.S.C. §112, second paragraph, for the recitation of the phrase "near a subsite," which was alleged indefinite.

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<sup>1</sup> As noted above with respect to claim numbering, the rejection properly refers to claim 4.

<sup>2</sup> Claim 8 was identified in the rejection although the basis for the rejection was not specified. Since Claim 8 recites the same "near a subsite" language found in Claim 4, Applicants assume that the basis for the rejection of Claim 8 is the same as for Claim 4.

Claim 33 was rejected under 35 U.S.C. §112, second paragraph as lacking antecedent basis for the term “lectin.”

Response

Although Applicants disagree with the rejection, Claim 4 has been amended to delete the phrase “near a subsite” and to instead refer to “a subsite comprising a substrate binding site of said enzyme, or in an amino acid position adjacent to the subsite or in van der Waals contact with the subsite.” This language clearly identifies the location of the amino acid residue to be substituted as described at, e.g., page 16, line 32 – page 17, line 2, of the original specification. Claim 8 has also been amended to delete the phrase “near a subsite.” Withdrawal of the rejections is respectfully requested.

Claim 33 has been amended to depend from claim 32, which provides antecedent basis for the term “lectin.” Withdrawal of the rejection is respectfully requested.

**IV. Claim Rejections under 35 U.S.C. §112, first paragraph**

Claims 9 and 10 were rejected under 35 U.S.C. § 112, first paragraph, as lacking written description for GenBank Accession Nos. that were incorporated by reference.

Claims 9 and 10 have been amended to delete the recitation of GenBank Accession Nos., thereby obviating the rejection.

Note that the absence of these GenBank Accession Nos. in the claims should not give rise to a future rejection asserting lack of written description for the recited polypeptides. It is well-established patent law that the fundamental question involved in a written description inquiry is “does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.” *In re Gotelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Here, Applicants make reference in the specification to well-characterized amino acid sequences maintained in a publically available database, which has been in existence for decades, and represents one of the fundamental tools for molecular biology research. In addition, as noted in Applicant’s previous Response, the Specification also provides a considerable amount of information about the structure of subtilisin type serine proteases. Given the amount of guidance provided in the Specification and what is known in the art, there is no doubt that a skilled person could identify the recited polypeptides and immediately locate the

recited amino acid positions. Therefore, the claims as amended fully comply with the written description requirement.

#### V. Claim Rejections under 35 U.S.C. §102

Claims 1-5, 8, 19-23, 25, 26, 32-34, and 36 were rejected under 35 U.S.C. § 102, as allegedly anticipated by Davis *et al.* (1998) *J. Org. Chem.* 63:9614-15. The rejection is traversed.

##### A. The Present Claims

The present claims, as exemplified by claim 1, are drawn to a catalytic antagonist of a target molecule, comprising a carbohydrate targeting moiety that specifically binds to the target molecule attached to a subtilisin-type serine protease, wherein the protease degrades the target molecule to reduce its binding to targeting moiety, resulting in the release of the antagonist, allowing it to bind and degrade another target molecule.

##### B. The Cited Reference

Davis *et al.* describe the site-selective glycosylation of a protein, which protein happens to be subtilisin from *Bacillus lenthus* (paragraph bridging columns 1 and 2 on page 9614). The reference is silent as to a catalytic antagonist or the mechanism underlying such a molecule.

##### C. Analysis

The standard for lack of novelty, that is, for anticipation, is one of strict identity. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d 1367, 231 USPQ 81, 90 (Fed. Cir. 1986); *In re Donohue*, 766 F2d 531, 226 USPQ 619, 621 (Fed. Cir. 1985). According to the MPEP at § 2131, “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.”

In the present case, the claims relate to a catalytic antagonist of a target molecule, comprising a carbohydrate targeting moiety that specifically binds to the target molecule attached to a subtilisin-type serine protease, wherein the protease degrades the target molecule to reduce its binding to targeting moiety, resulting in the release of the antagonist, allowing it to bind and degrade another target molecule. In contrast, the teachings of Davis *et al.* are limited to the site-specific glycosylation of a polypeptide. The polypeptide happens to be a subtilisin, although it is apparent from reading the reference that the polypeptides could have been any polypeptide. Nowhere do Davis *et al.* teach that that site-specific glycosylation of a polypeptides can be used to target the

polypeptide to a preselected target molecule, that the subtilisin component of the glycosylated polypeptides can be used to degrade a target molecule, or that a glycosylated subtilisin can function in a catalytic manner, allowing it to degrade more than one target molecule. All these features are expressly required by the present claims, and none of the features are described by Davis *et al.*

Neither do Davis *et al.* inherently anticipate the present claims. Inherent anticipation requires that the alleged inherent feature necessarily be present in a prior art reference – inherency cannot be established by mere probability. *Continental Can*, 948 F.2d 1264, 20 U.S.P.Q.2d (BNA) 1746 (Fed. Cir. 1991). Davis *et al.* do not teach a particular carbohydrate moiety for binding to a target molecule, that the glycosylated polypeptide would bind to a target molecule, that the glycosylated polypeptide would degrade a target molecule, or that the glycosylated polypeptides would be regenerated and made available to degrade an additional target molecule. None of these features necessarily follow from what is described in Davis *et al.*; therefore, the reference does not inherently anticipate the present claims.<sup>3</sup>

Since Davis *et al.* neither expressly or inherently anticipate the present claims, withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.

## VI. Claim Rejections under 35 U.S.C. §103

Claim 35 was rejected under 35 U.S.C. § 103, as allegedly obvious over Davis *et al.* (1998) *J. Org. Chem.* 63:9614-15 in view of Nilsson *et al.* (1997) *Glycoconjugate J.* 4:219-23. The rejection is traversed.

### A. The Present Claims

The present claims, as exemplified by claim 1 are summarized above. Claim 35 depends from claim 1, and further requires that the targeting moiety is thioethyl D-mannopyranoside.

### B. The Cited Reference

Davis *et al.* are described above.

Nilsson *et al.* teach the synthesis of a dimeric Lewis-x hexasaccharide as a *p*-trifluoroacetamidophenylethyl- $\beta$ -glycoside.

### C. Analysis

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<sup>3</sup> The Examiner at page 4 of the Office Action makes reference to additional knowledge that is allegedly well-known in the art. However, a combination of references is appropriate in the case of an obvious rejection, not an anticipation rejection.

Claim 35 depends from claim 1. As described above, claim 1 includes features that are nowhere taught or suggested by Davis *et al.* Nilsson *et al.* do not correct the defect in Davis *et al.* with respect to claim 1. Since neither Davis *et al.* nor Nilsson *et al.*, separately or in combination, teach or suggest the features of claim 1, it is immaterial whether Nilsson *et al.* teach the additional limitation of claim 35.

For at least these reasons, withdrawal of the rejection under 35 U.S.C. § 103 is respectfully requested.

### CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe the present application is fully in condition for allowance. Issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7595.

The Commissioner is authorized to charge any fees that may be required in connection with this submission and to credit any overpayments to Deposit Account No. 07-1048.

Respectfully submitted,

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